Ohio Opioid Technology Challenge: Topic 2 'Prevent' - Webinar Transcript

Speakers:

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Date of Webinar: 05/17/2017
Time of Webinar: 10:00 AM – 11:00 AM Eastern

Jonathan Jakischa: Good morning to you all and welcome to today's webinar for the Ohio Opioid Technology Challenge Topic 2: Prevent brought to you by NineSigma. My name is Jonathan Jakischa from NineSigma and I'll be your host and moderator today. Please note that this webinar is being recorded, the recording and transcription will be made available on the Ohio Opioid Technology Challenge page.

Let's review our agenda for today. After I introduce our speakers, they will begin to discuss this project in greater depth including an overview and some frequently asked questions. We'll conclude by addressing your questions during the live Q&A session followed by a brief summary of project information including how to request additional information or assistance. As we proceed through today's presentation please feel free to ask your questions at any time. We'll keep track of your questions and respond to them during the Q&A session of today's webinar. Should you need any additional information or assistance outside of today's webinar please feel free to contact the NineSigma Provider Help Desk, and I'll have that email for you at the end of today's presentation.

At this time, I'd like to introduce our guests for today's webinar. First, we're joined by Joe Kitzmiller MD, PhD, FCP from the Ohio State University Medical Center College of Medicine. From NineSigma we're joined by Kevin Andrews PhD, senior program manager. Gentlemen, thank you both for joining us today.

Joe Kitzmiller: Thank you.

Jonathan Jakischa: Great. We'll begin with Kevin Andrews from NineSigma. Kevin, could you please give our attendees an overview of this particular challenge topic?

Kevin Andrews: Sure. Thanks. The challenge is a three-phase prize-based competition to find technology-based solutions that address the opioid crisis through either addiction prevention and treatment, or overdose avoidance, or overdose response.

This three-phase challenge, we're in the second phase. The first phase was the Idea Phase, we're now in the phase 2; the Challenge Phase. This phase has up to 12 $200,000 prizes. The Challenge Phase winners will then be able to compete

in phase 3, the Product Phase with a submission in July 2019, and there will be up to four $1-million prizes for those 12.

The Ohio Opioid Technology Challenge consists of four topics broadly themed diagnose, prevent, connect, and protect. The focus of today's webinar is Topic 2, Prevent. With that I present Dr. Joe Kitzmiller who will provide context related to this topic.

Joe Kitzmiller: Hello everybody, can you hear me okay?

Jonathan Jakischa: Yes Joe, please proceed.

Joe Kitzmiller: Great. This is the Ohio Opioid Technology Challenge: Prevent. The goal, again, is to have technology solutions to include diagnostics, sensors, medical devices, pharmaceutics and health informatics systems to reduce urges, cravings, or other symptoms of opioid withdrawal.

I'm going to be presenting the current state of affairs regarding prescription pharmacologic treatment options. I'll also discuss some non-prescription options, as well as some non-pharmacologic treatment options. We're also going to discuss the potential role of pharmacogenomics of opioids as well as of treatments to reduce urges, cravings or symptoms of withdrawal. Also, going to discuss and provide examples of some bioinformatics approaches, as well as some diagnostics. Next slide please.

The current prescription pharmacologic treatment options include, of course, naloxone, the brand name Narcan. As we all are likely aware, this is used for the treatment of overdose, so basically opioid overdose occurs primarily because too much opioid is activating the new receptors and the other opioid receptors to cause respiratory depression. Meaning that your normal person has, say, 15 respers per minute, as you increase the doses of Opioid that goes from 15 to 14, 12, likewise until you get to about 6 respers per minute. At that point, the central nervous system no longer renews the breath, so that's not the exclusive reason for opioid death, or opioid overdose death, but that is the primary mechanism of death. Again, Narcan and naloxone reverse that.

Prescription pharmacologic treatments for cravings and urges, so Buprenorphine, as well Naltrexone, that combined is called Suboxone, that's one of the trade names. This is used in many addiction clinic, again, to treat cravings and urges, to reduce that.

Treatment for withdrawal symptoms, so when somebody's taking an opioid for a long period of time, or regular use of opioid, as we mentioned, you start to have these issues such as CNS depression, respiratory depression, so automatically when they withdraw the symptoms are opposite of that, so that's why they will have high blood pressure, high heart rate, a higher risk of seizure, as well as they often have diarrhea because the opioid itself causes

constipation. You may have seen the commercials for opioid induced constipation, so it causes constipation, so when they withdraw they have the opposite of constipation—they have diarrhea. The pharmacological treatments for withdrawal symptoms include the antidiarrheals, the antihypertensives, as well as antiseizure medications.

In addition, there are some prescription pharmacologic treatment options that are considered ... they're definitely for temporary use, and they're considered to safer substitutes to some of the stronger opioids. These include methadone, which itself is still an opioid, it is still addictive, but it's a much less concentration, or powerful. It's much less potent than opioids such as, again, heroin, et cetera, or morphine. There are still methadone clinics and, again, what they do is they have the patients, off of their strong narcotics, and take methadone for a couple of months, and they'll slowly wean down that dose. Again, the advantages there is at least the patients know how much they're getting, and they know that it's a pure drug.

Other temporary safer substitutes, so medical marijuana has been proposed as potentially safer, and a way to help patients with opioid addiction at least come off their opioid. Let's go ahead and read this disclaimer here because we want to make it very clear that we, myself Dr. Joe Kitzmiller as well as NineSigma, we are not endorsing the use of medical marijuana. Let's read this: so peer-reviewed scientific articles and data support the efficacy of naloxone, methadone, and buprenorphine/naltrexone. This type of data has not been reported for medical marijuana. Medical marijuana is not legal in many states, and it's important to note that federal law, the US FDA and the DEA have not recognized or approved medical marijuana. They just, at this point, are choosing not to necessarily enforce that federal law, and that could change at any time. Again, neither NineSigma nor myself endorse the use of medical marijuana as a treatment option for opioid craving, urges or withdrawal. Next slide please.

Some of the nonprescription options and, again, we're not going to be endorsing any of these I just wanted to discuss these because these are nonprescription medications that many of our patients may be using in conjunction with the other methods, or by themselves.

One is the Tai-King-Ning. Another is ginseng, another is U'finer, and the other one, Kratom, that's M. Speciose is the scientific name for Kratom, that's a plant. Again, these have been purported to help with opioid addiction. Our disclaimer here is first of all, this is not an exhaustive list of the purported nonprescription options. These non-traditional options many of them are based in Chinese medicine, have little data to support their efficacy, but there's plenty of anecdotal evidence suggesting that there may be release of cravings, urges and withdrawal symptoms, and most importantly, our patients may be taking these. There are problems with unregulated preparations, and unknown purity, as well, those are large concerns. Also, again, Federal and State laws may limit the use of any one of these. Again, neither NineSigma nor myself endorse the use of

these non-prescription, non-traditional, unregulated therapies. Next slide please.

Some non-pharmacologic treatment options for opioid addiction or prevention. Certainly, the 12-step programs, so that would be Narcotics Anonymous when we're talking about opioids. These programs have been around for 60 or 70 years, and they were actually started in Ohio up in the Canton, Ohio area. The success of the 12-step programs cannot be understated. These are very, very powerful programs.

In addition, there are many cognitive behavioral therapy protocols specific for addiction that a counselor or psychiatrist can use. Acupuncture has been purported to also help with addiction cravings, and meditation or mindfulness is also meant to help with cravings and urges. Note here, this is not an exhaustive list. Some of these do have some proven success as adjuncts and/or standalone treatment for the ... I'm sorry, adjuncts to the prescription pharmacologic treatments for craving, urges and withdrawal symptoms. As well as some proven success as standalone treatment options. Next slide please.

Pharmacogenomics, I just want to introduce this topic. This is my area of expertise, I do pharmacogenomics in the cardiovascular space, however, I have done some review articles on addiction specifically in pharmacogenomics, so you can look up Kitzmiller addiction, and pharmacogenomics, you could Google that and find an article that was recently published, I believe it was by Gavin Publishers.

The idea here, pharmacogenomics is based on using patient's genetics to determine either their disease risk, so in this case it would be are they at high risk for opioid dependency or abuse? It can also be used to help us understand how they would process opioids, so we would look at genetic variants in the metabolizing enzymes, and that could lead us to say, "If we're going to prescribe this patient Oxycontin we should do a low dose because they don't metabolize it well, so we need to keep the doses low." It can also inform us ... Some of the metabolizing enzymes for coding are different from the ones that are for, again say, Oxycontin or methadone so, again, it can help us select which opioids are most appropriate, as well as what dose is most appropriate for a patient.

Genetic biomarkers can also inform us regarding the pharmacologic treatments of our opioid urges, cravings and withdrawal symptoms. Again, the medicines like ... probably not Narcan because we give everyone the same dose there to make sure it works, but some of the other ones like Suboxone, or methadone those have certain metabolizing enzymes and transport enzymes specific to those treatment options that there could be genetic variation, polymorphisms, that may, again, help us determine at least dose selection to have optimal outcome for those patients. As well as, there could be markers that tell us that, again, Suboxone is a good option for this type of patient, they're likely to have a good response. That's some areas that could be further developed as far as pharmacogenomics. Next slide please.

Also, want to talk a little bit about bioinformatics, that's another area of my expertise. There are many large data sets, and these data sets have been funded by NIH projects, that's why they need to be publicly available. There's these large data sets that exist that include patient demographics, various clinical variables, medication use including opioid use, and/or the related morbidity and mortality. These large databases could be used or can be used to identify variables, these could be clinic variables, demographics, or pharmacogenomic variables to predict opioid dependency risk, or response to the pharmacotherapies that we've discussed for reducing cravings, urges and withdrawal. In addition, bioinformatics technology, bioinformatics approaches also could provide opportunity to potentially integrate patient electronic medical records with systems like the Ohio Automated Rx Reporting System and/or other systems. Next slide please.

Another topic I wanted to touch on is diagnostics. Currently, all patients that are enrolled in a treatment program for opioid abuse are required to abstain from illicit opioid use, and they often have routine and random drug screens in order to stay in a treatment program. This is done, again-

Jonathan Jakischa: My apologies everyone. We seem to have lost Dr. Kitzmiller for just a moment. Everyone please stand by. Dr. Kitzmiller, can you hear me? Again, to our attendees, I apologize for the interruption. It appears we have lost Dr. Kitzmiller for the moment.

With that in mind, I think we'll proceed with today's webinar and, hopefully, Dr. Kitzmiller will be able to rejoin us a little bit later in the webinar.

Turning now back to Kevin Andrews from NineSigma. Kevin, could you tell our attendees a little bit more about what sort of information they should include in their responses, how responses will be evaluated, and other such information?

Kevin Andrews: Sure. Minimum requirements for submissions your approach must use technology as a component. The technologies can include sensors, diagnostics, medical devices, pharmaceuticals, and/or health information technology. You can also involve software, but really only in conjunction with the above technologies. You should already be working on your approach. This is not a call for an idea or a concept. You need to have efforts underway. You should have proof of concept with compelling data that supports the effectiveness of your approach. You should have a clear plan and path forward to get your technology ready for broad deployment or implementation. Your approach must be able to be implemented in the United States. It should be likely to receive regulatory approval, and you need to be able to demonstrate your approach in conjunction with an Ohio-based entity.

There are some approaches that are listed as ineligible, these do not qualify for any of the technology challenge topics. Approaches that are strictly at an early stage of concept—an early concept stage of development—are ineligible. Any solution that requires a change in current law, policy, or regulation, also not

qualified. Clinical treatment protocols that are not associated with a new technology development are not qualified. Alternative pain management therapies are not of interest. Predictive analytics to inform public policy, programs for the delivery of a social or clinical point-of-care service that does not have a significant technology component is not eligible. Education and public awareness programs, and professional training programs are not eligible.

What are the general evaluation criteria that the evaluators will use to determine winners? You should consider how your approach aligns with the key out to be for the topic, which I'll get into momentarily. Your technology maturity and time to market. So for similar approaches preference will be given to the approach that is more mature, and/or that has a shorter time to market. The potential for broad deployment or implementation, the size or scope of the audience impacted, the so-called market size, the robustness of your approach, and the effectiveness of your approach, those are all evaluation criteria.

In terms of this topic, Topic 2, the key attributes are as follows: your approach should reduce urges, cravings, or other symptoms of withdrawal. Your approach should offer lasting effects over time. Your approach should not pose other significant health risks, and your approach should preferably be in a later stage of development. In the case of a pharmaceutical we prefer that it at least be in human clinical trials, and for a medical device preferably you have received the 510(k) clearance.

What possible approaches might be considered? Approaches may include, but are not limited to, pharmaceuticals or medical devices that address predictive responses.

What do you need in your proposal, your response submission? This chart outlines the sections, the elements of your response. I'm not going to read through them, this is also listed in the challenge summary for the topic on our webpages. Please pay attention to the page limit, you may also include a link to video, and upload supporting documents as appropriate.

The timeline is also something you want to pay attention to. The Challenge Phase launched in February, we are here today with the webinar on May 17, the submission deadline is July 11th at 5 PM Eastern Daylight Time. The Challenge Phase prize recipients will be announced on September 18, the Product Phase will begin in September and go through July 2019, and the post-Product Phase, the post-Challenge Phase will commence after that and go into 2021.

Jonathan Jakischa: Great. Thank you, Kevin. For our attendees, it's now time for the frequently asked questions. Now, these are questions that have already been asked via the NineSigma provider help desk or are general questions but NineSigma projects. We'll go through these questions one at a time.

Our first question, Kevin, could you please explain what you mean when you say that an entrant must be registered to do business and be in good standing with the State of Ohio?

Kevin Andrews: Sure. Regarding registration there is a website with the State of Ohio where there are forms that you can complete. A non-Ohio entity would choose Form 530A, if they are a for-profit entity, and Form 530B for nonprofit. The registration fee is $99 US.

Jonathan Jakischa: Our next question. When do I need to register to do business in Ohio, prior to submitting a response or before accepting an award, if I'm chosen to receive an award?

Kevin Andrews: You do not need to register to do business in Ohio in order to submit a challenge response. If your submission is selected as a winner, you would need to register to do business in Ohio before accepting the award.

Jonathan Jakischa: Thank you. Our next question. Who is eligible to compete for the Product Phase?

Kevin Andrews: Only winners of the Challenge Phase will be eligible to compete in the Product Phase.

Jonathan Jakischa: Do I have to fill in each section of the online response form or can I prepare my submission as an attached document?

Kevin Andrews: You can do either. We ask that you please pay attention to the list of elements required, that slide How to Submit Elements of Your Response. Please adhere to the page limits, and remember that you are allowed to upload supporting documents.

Jonathan Jakischa: What is required of Challenge Phase winners to be able to compete for Product Phase awards?

Kevin Andrews: Challenge Phase winners are going to be required to execute a nondisclosure agreement with NineSigma and submit a more detailed plan that explains tasks, timeline, and deliverables. The plan that you plan to follow to continue development of your technology for deployment or commercialization. You're also going to need to explain how you're going to involve an Ohio in-state entity in your effort. Then, during the period from approximately October 2018 to July 2019, you will work against that plan.

Jonathan Jakischa: Our next and, I believe, our final question. What will be required of Product Phase winners after they accept their award?

Kevin Andrews: Winners of the Product Phase will be obligated to deliver periodic reports to NineSigma from Q4 of 2019 through Q4 of 2021. NineSigma will ask you to

provide some information that may be disclosed to the State of Ohio, and other information will remain confidential. Further details will be available when the Product Phase starts.

Jonathan Jakischa: Great. Thank you, Kevin.

Now, at this time, we'll open up the session to questions from our attendees. Please submit your questions via the question box on your screen. This is an excellent opportunity for you to pose your questions directly to our speakers. We'll take the rest of our time today to go through those questions and answer them live. If we don't get to your question don't worry, any questions that we receive but aren't able to get to today will be addressed as part of the transcript that will be made available on the challenge page shortly. If you think of a question that is not conceived of during today's webinar don't worry, we'll have some additional information for you in upcoming slides for where you can pose that question to us, and we will do our best to get to the information that you're seeking.

At this time, our very first question. This is probably best addressed by Kevin from NineSigma. Kevin, can you expand what you mean by an Ohio entity?

Kevin Andrews: Yes. If you look at the official rules for the Challenge Phase, section 5.3 for purposes of this challenge, an in-state entity is one that has a substantial presence in Ohio, and there's reference to the Ohio Revised Code section 184.10. Please refer to that for more detail. Basically, the idea is that the entity has to be doing business or conducting activity within the State of Ohio, so if you are someone from outside of Ohio, or even outside of the United States when you get to working on your effort to compete ... Let's say, you are awarded a Challenge Phase award in order to compete for the Product Phase award you will have to identify, and engage an in-state Ohio entity as part of your program. You don't necessarily have to have that worked out in order to submit for the Challenge Phase, but you need to have a plan to get that collaboration in place should you be selected as an award winner of the Challenge Phase.

Jonathan Jakischa: Great. Our next question. Would a technology that prevents addiction in the first place be of interest?

Kevin Andrews: I guess, strictly speaking, that might not be in scope. On the other hand, if you're saying that you have an approach that eliminates symptoms of withdrawal because they don't exist maybe that would be considered.

Jonathan Jakischa: I think this next question builds a little bit off of what you were just saying Kevin. Would a technology that could detect early indicators of withdrawal symptoms be of interest?

Kevin Andrews: In the sense that that technology could be used as a cue to maybe administer or indicate that some other substance, or protocol be started, for example, some kind of wearable technology that might indicate the onset of withdrawal symptoms yeah, that could be useful because then you could potentially address the withdrawal symptoms before they became severe.

Jonathan Jakischa: Our next question. Is there a target duration? I think what the question here is trying to get at is, is there a minimum amount of time that a solution should address those withdrawal symptoms?

Dr. Kitzmiller, can you provide some context for duration may be in the context of time between doses of medically-assisted treatment?

Joe Kitzmiller: Sure. Pharmacologic treatment, so Suboxone, again, that is a commonly used pharmacologic treatment for cravings, and urges. I believe Suboxone can be prescribed daily or as a twice-daily medication. We talked about substitute, again, the methadone clinics. Methadone is typically dosed, I believe, twice a day, although, there may be a single once a day formulation. Does that answer the question? Is that what you're asking, Sir?

Jonathan Jakischa: Yeah, I think so. I think, what people are trying to understand is what's reasonable for how long whatever this technology-based solution is to address withdrawal symptoms and what's-

Joe Kitzmiller: I think I understand. Withdrawal symptoms, opioid withdrawal is typically confined within a week. Obviously, the symptoms are most ... I shouldn't say prevalent, but the strongest, probably I would say typically, about 6 to 12 hours to 24 hours after the last opioid use. That's when the withdrawal symptoms really kick in.

The withdrawal symptoms are very dangerous, I covered some of the more basic ones such as, again, the high blood pressure because the heart rate, and heart rate are going up, as well as the diarrhea, which is typically pretty severe. Most importantly, I think, is that the third one, which is the seizures. Both alcohol and opioid are the only sym ... I'm sorry, the only drugs of abuse that withdrawal can lead to seizure, which can be life threatening. Again, that's typically confined within a week. I think we say that the seizure risk is about 72 hours, but we've seen seizure beyond that. I would say confined within a week. Does that answer your question?

Jonathan Jakischa: Yes. Dr. Kitzmiller, I think we're going to stick with you for just a moment here. Our next question. In your opinion, which is the more important aspect, how rapidly a method can provide withdrawal symptom relief or how long a duration it provides that relief?

Joe Kitzmiller: If, again, we're talking about treatment for withdrawal specifically that's going to be a treatment whether it's pharmacologic or other treatment that's only

going to be used during that first. Then so, now we're talking about does it matter if they take the medicine or the treatment and it works for the withdrawal symptoms within 10 minutes, or an hour, or if it takes a couple of days of dosing.

Obviously, it's definitely better if it's quicker, of course. If it lasts longer that can be important because if it doesn't last long then it's something that you have to do every 6 hours, every 12 hours, every 24 hours, so if you have something that is at least a daily dosing, or even extended beyond that, that would be ideal as well because then these patients who are in withdrawal they're often indigent not always, and they may not be able to continue to make it to the pharmacy and/or their clinic. If you had a preparation that would handle the withdrawal symptoms for quite some time that would be helpful.

Most people do their withdrawal in a clinical setting such as an addiction treatment center, so in that respect it's not terribly important because they can get the treatment as needed. However, for our folks that are withdrawal in prison, or at home there could, certainly, be some advantages to having something, a treatment that's lasts longer. Both are important. I think most important may be how quick it can help with withdrawal.

Jonathan Jakischa: I think our next question Dr. Kitzmiller is probably best, again, addressed to you. In your opinion, would it be more effective if a technology or approach could completely address one single withdrawal symptom or would it better if an approach to partially address multiple different withdrawal symptoms?

Joe Kitzmiller: There are certainly advantages to a treatment that can treat multiple withdrawal symptoms, that would certainly be a very worthwhile product. There's definitely some challenges to that, but yeah, that would be wonderful, but it is important that it's effective. That's probably the most important thing, that it's effective in treating the withdrawal symptoms even if it's only one it needs to be effective.

Again, there's a hierarchy when we talk about what's important here with withdrawal, with the number one being definitely the seizure control, and the hypertension control because those can be life-threatening. Other things where my skin is crawling, or diarrhea those are very unfortunate, but they're not as life-threatening, and as important as the two former ones I mentioned.

Jonathan Jakischa: Great. Thank you Dr. Kitzmiller. Our next question. Would a technology that could proactively dispense compounds to combat the symptoms of interest? Kevin-

Joe Kitzmiller: Yes. Yes, that would be.

Jonathan Jakischa: Great. Thank you for that very succinct answer, Dr. Kitzmiller.

Our next question, and actually before I get to our next question I just want to reiterate to our intent in the attendees today, if you have a question for either of our speakers please feel free to submit it. This is a great opportunity for you to get feedback to your questions very, very promptly. Like I said, if you think of a question outside of the webinar please don't worry about it. In our next slide I'll have some information about how you can get information that you're seeking. Our next question. Would an analgesic compound that has a lower addictive potential also be of interest?

Kevin Andrews: This is Kevin. From the prospect of medical treatment it's of interest, however, in the context of this particular challenge topic I believe it's not in scope.

Joe Kitzmiller: I could add to that, that really it would have to be combined ... I think we've discussed this. It would have to be combined with some type of novel technology, is that correct Kevin?

Kevin Andrews: Yes.

Jonathan Jakischa: We're seeing a bit of a slowdown in the questions that are coming in. We've got, I think, one more to go through. After this next question, after our speakers address it we'll wait just a moment or two to see if we have any additional questions, if there aren't I'll proceed to close out today's webinar.

With that in mind, proceeding to our next question. Would a technology that makes use of existing genetic databases to make predictions regarding the addictive potential of a pharmacological chemical be of interest? Dr. Kitzmiller, maybe this one would be best addressed by you.

Joe Kitzmiller: I think, again, if you have a bioinformatics technology, so that maybe some type of computer program, or something whereby you're going to access these large databases on an ongoing basis, so that as the databases either add themselves, or other ones are added in, and you have a way to continually check, to look at these data sets, and look at the clinical variables, the genetic variables, as well as opioid use and abuse, as well as use of pharmacological treatments for urges, cravings, and withdrawal, and also have some kind of clinical outcome measures, if you had a technology that could incorporate that type of stuff, and provide information back to not the community, but the opioid prevention scientific community I would think that would be very important. Kevin, you might want to clarify.

Kevin Andrews: Thanks. I think while it might be interesting the focus of this challenge, of course, is to find technologies that help patients directly. I think one would have to think a little bit about how to use this knowledge to affect treatment of individuals.

Jonathan Jakischa: Gentlemen, thank you both for that answer. At the moment, it looks like we don't have any further questions coming in, so with that in mind, I will proceed to our next slide and wrap things up.

To our attendees, what can you do today? First and foremost, obviously, you can visit the challenge page. The URL for the challenge page is right there on your screen right now. It's ninesights.ninesigma.com/web/topic2, and that will take you to this particular topic page, so you can learn more about the challenge, what's in scope, and what's not, and you could also access the response form while you're there. Additionally, while you're on NineSights you can subscribe to receive updates for the project, view FAQ documents, you can also join the community.

Now, as I mentioned previously, if you have questions outside of today's webinar and you want to get information about this particular topic, or the Ohio Opioid Technology Challenge more broadly you can reach out to the NineSigma Solution Provider help desk, and there's two ways to go about doing that. First, you can obviously, reach us via email it's grandchallenge@ninesigma.com, that email address once again is grandchallenge@sigma.com. Alternatively, you can reach us by phone at 216–283–3914, that phone number once again, 216-283-3914. If you've got questions about what may or may not be in scope, if you need assistance with your submission, whatever assistance we can help provide to you please feel free to reach out. More than happy to provide assistance and information as needed.

Last, and certainly very importantly, **the deadline for submissions is Wednesday, July 11, 2018 at 5 PM Eastern Time**, please make sure that you get your submissions into us in advance of that 5 PM deadline. We aren't able to accept any late submissions, so get your submission in advance of that 5 PM deadline.

To our panelists today, gentlemen, thank you very much for your time. We appreciate your insight into this topic. To our attendees, thank you very much for joining us today. We appreciate you listening to us speak. We look forward to seeing your submissions. Thank you all once again, and have a great day.